09/ 634,207

Welcome to STN International! Enter x:x

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS	4	DEC 08	INPADOC: Legal Status data reloaded
NEWS	5	SEP 29	DISSABS now available on STN
NEWS	6	OCT 10	PCTFULL: Two new display fields added
NEWS	7	OCT 21	BIOSIS file reloaded and enhanced
NEWS	8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS	9	NOV 24	MSDS-CCOHS file reloaded
NEWS	10	DEC 08	CABA reloaded with left truncation
NEWS	11	DEC 08	IMS file names changed
NEWS	12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS	13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS	14	DEC 17	DGENE: Two new display fields added
NEWS	15	DEC 18	BIOTECHNO no longer updated
NEWS	16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS	17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS	18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS	19	DEC 22	ABI-INFORM now available on STN

NEWS EXPRESS	DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:20:13 ON 06 JAN 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:20:22 ON 06 JAN 2004

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 JAN 2004 HIGHEST RN 634558-38-6
DICTIONARY FILE UPDATES: 5 JAN 2004 HIGHEST RN 634558-38-6

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

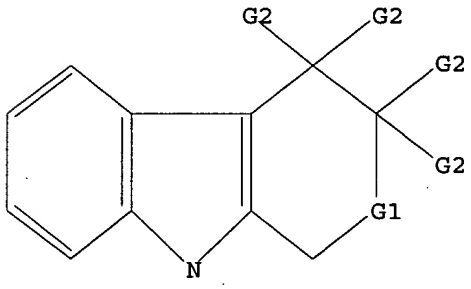
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading 09634207.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S
G2 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful
FULL SEARCH INITIATED 13:20:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6947 TO ITERATE

100.0% PROCESSED 6947 ITERATIONS 1256 ANSWERS
SEARCH TIME: 00.00.01

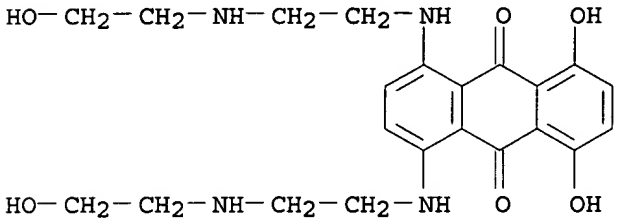
L2 1256 SEA SSS FUL L1

=> s mitoxantrone
L3 6 MITOXANTRONE

09/ 634,207

=> d scan l3

L3 6 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]- (9CI)
MF C22 H28 N4 O6
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

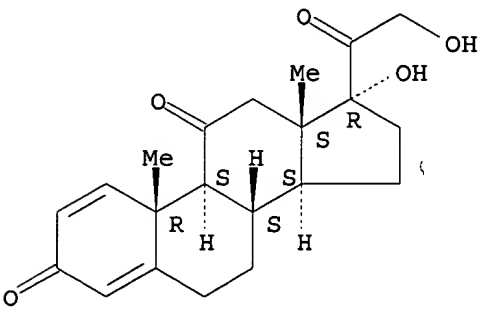
=> s prednisone
L4 40 PREDNISONE

=> d scan l4

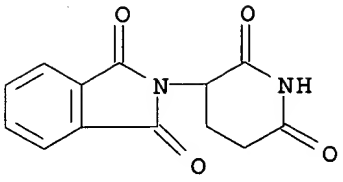
L4 40 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-, mixt. with 2-(2,6-dioxo-3-piperidinyl)-1H-isoindole-1,3(2H)-dione (9CI)
MF C21 H26 O5 . C13 H10 N2 O4
CI MXS

CM 1

Absolute stereochemistry.



CM 2



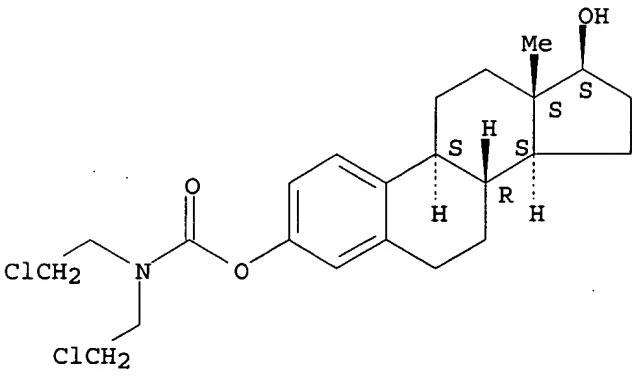
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s estramustine
L5 13 ESTRAMUSTINE

=> d scan l5

L5 13 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Estra-1,3,5(10)-triene-3,17-diol (17.beta.)-, 3-[bis(2-chloroethyl)carbamate] (9CI)
MF C23 H31 Cl2 N O3
CI COM

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

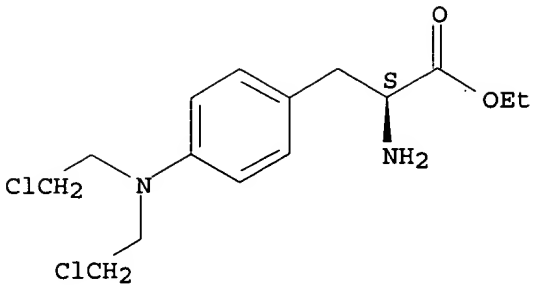
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s melphalan
L6 17 MELPHALAN

=> d scan l6

L6 17 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN L-Phenylalanine, 4-[bis(2-chloroethyl)amino]-, ethyl ester (9CI)
MF C15 H22 Cl2 N2 O2
CI COM

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

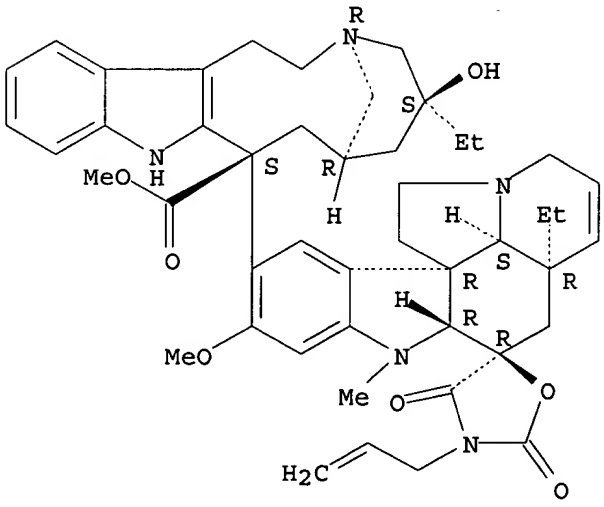
=> s vinblastine
L7 155 VINBLASTINE

=> d scan l7

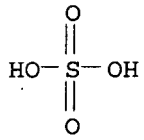
L7 155 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 2H-3,7-Methanoazacycloundecino[5,4-b]indole-9-carboxylic acid, 9-[(2.beta.,3.beta.,5.alpha.,12R,19.alpha.)-6,7-didehydro-16-methoxy-1-methyl-2',4'-dioxo-3'-(2-propenyl)spiro[aspidospermidine-3,5'-oxazolidin]-15-yl]-5-ethyl-1,4,5,6,7,8,9,10-octahydro-5-hydroxy-, methyl ester, (3R,5S,7R,9S)-, sulfate (1:1) (salt) (9CI)
MF C47 H57 N5 O7 . H2 O4 S

CM 1

Absolute stereochemistry.



CM 2



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

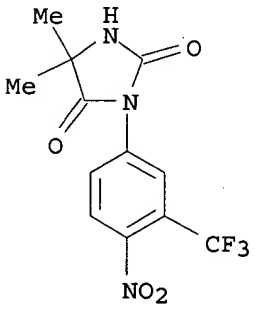
```
=> s bicafutamide
L8            0 BICAFUTAMIDE

=> s bicaflutamide
L9            0 BICAFLUTAMIDE

=> s nilutamide
L10           1 NILUTAMIDE

=> d scan l10

L10  1 ANSWERS   REGISTRY  COPYRIGHT 2004 ACS on STN
IN   2,4-Imidazolidinedione, 5,5-dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]-
      (9CI)
MF   C12 H10 F3 N3 O4
CI   COM
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

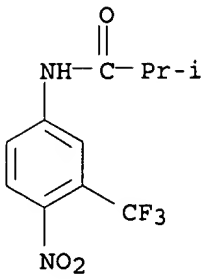
ALL ANSWERS HAVE BEEN SCANNED

```
=> s flutamide
L11           5 FLUTAMIDE

=> d scan l11

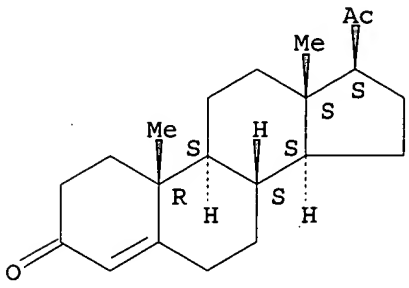
L11  5 ANSWERS   REGISTRY  COPYRIGHT 2004 ACS on STN
IN   Pregn-4-ene-3,20-dione, mixt. with 2-methyl-N-[4-nitro-3-
     (trifluoromethyl)phenyl]propanamide (9CI)
MF   C21 H30 O2 . C11 H11 F3 N2 O3
CI   MXS

     CM   1
```



CM 2

Absolute stereochemistry.



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	[redacted]	[redacted]

FILE 'CAPLUS' ENTERED AT 13:26:29 ON 06 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 6 Jan 2004 VOL 140 ISS 2
FILE LAST UPDATED: 5 Jan 2004 (20040105/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 13:20:13 ON 06 JAN 2004)

```
     FILE 'REGISTRY' ENTERED AT 13:20:22 ON 06 JAN 2004
L1              STRUCTURE UPLOADED
L2         1256 S L1 FUL
L3            6 S MITOXANTRONE
L4           40 S PREDNISONE
L5           13 S ESTRAMUSTINE
L6           17 S MELPHALAN
L7          155 S VINBLASTINE
L8            0 S BICAFUTAMIDE
L9            0 S BICAFLUTAMIDE
L10           1 S NILUTAMIDE
L11           5 S FLUTAMIDE

     FILE 'CAPLUS' ENTERED AT 13:26:29 ON 06 JAN 2004

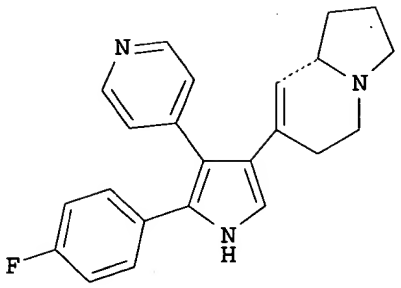
=> s l2
L12         700 L2

=> s l12 and (carbonyl or carboxyl or sulfonyl or sulphonyl)
        153336 CARBONYL
         62752 CARBOXYL
         26512 SULFONYL
            44 SULPHONYL
L13          4 L12 AND (CARBONYL OR CARBOXYL OR SULFONYL OR SULPHONYL)

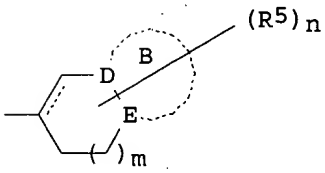
=> d l13 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

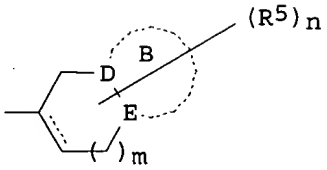
L13  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:793467  CAPLUS
DOCUMENT NUMBER:          137:310916
TITLE:                    Preparation of (hexahydroindolidinyl)pyrrole,
                          -thiophene, -pyrazole, and -imidazole derivatives as
                          cytokine production inhibitors and their novel
                          medicinal use in combination with nonsteroidal
                          antiinflammatory agents
INVENTOR(S):              Ushiyama, Shigeru; Kimura, Tomio
PATENT ASSIGNEE(S):       Sankyo Company, Limited, Japan
SOURCE:                   PCT Int. Appl., 521 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

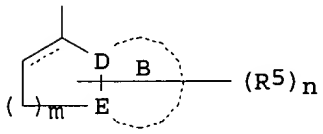
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2002080974      A1   20021017      WO 2002-JP3354   20020403
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     JP 2002363104      A2   20021218      JP 2002-101720   20020403
PRIORITY APPLN. INFO.:                  JP 2001-105615   A  20010404
OTHER SOURCE(S):          MARPAT 137:310916
GI
```

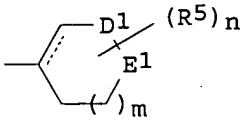


II

Q= 

Q1= 

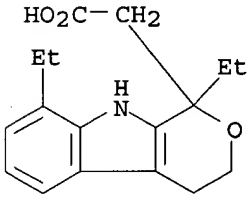
Q2= 

Q3= 

AB Disclosed is a drug having relieved side effects of a nonsteroidal antiinflammatory agent (NSAID) which is to be used for simultaneously, sep., or intermittently during administering the nonsteroidal antiinflammatory agent, in particular having cyclooxygenase inhibitory activity, with an inflammatory cytokine prodn. inhibitor. The active ingredient of the inflammatory cytokine prodn. inhibitor is a compd. represented by the general formula R1R2A-R3 [I; wherein A = an (un)substituted trivalent group selected from benzene, pyridine, pyridazine, pyrimidine, pyrrole, furan, thiophene, pyrazole, imidazole, isoxazole, and isothiazole; R1 = each (un)substituted aryl or heteroaryl; R2 = (un)substituted heteroaryl contg. at least one N atom; R3 = Q-Q3; wherein m = 1,2; n = 1-3; R5 = H, HO, NO2, cyano, halo, lower alkoxy, halo-lower alkoxy, lower alkylthio, lower alkyl, lower alkenyl, lower alkynyl, aralkyl, oxo, hydroxyimino, lower alkoxyimino, lower alkylene, etc.; one of D and E is N and the other one is (un)substituted CH; one of D1 and E1 is (un)substituted NH and the other one is (un)substituted CH2; the ring B contg. D and E = a 4- to 7-membered heterocyclic ring optionally fused with aryl, heteroaryl, cycloalkyl, or heterocyclyl group; a proviso is given]. The above compd. alleviates the side effects, in particular stomach mucus membrane injury such as erosion or ulcer, of NSAID having cyclooxygenase inhibitory activity such as Aspirin, Etodolac, Diclofenac sodium, Aceclofenac, Indometacin, Farnesol, Nabumetone, Ibuprofen, Ketoprofen, Loxoprofen sodium, Naproxen, Nimesulide, Oxaprozin, Zaltoprofen, Piroxicam, Lornoxicam, Meloxicam, Celecoxib, Rofecoxib, Valdecoxib, and Etoricoxib. The above drug is useful for prevention or treatment of inflammations, malignant tumors, Alzheimer's disease, chronic articular rheumatism, or arthritis. Thus, 1-(4-fluorophenyl)-3-(4-pyridyl)-4-(1,2,3,5,6,8a-hexahydroindolizin-7-yl)pyrrole (II) at 30 mg/kg inhibited by 91% the injury of stomach mucous membrane induced by Diclofenac sodium (15 mg/kg) in rats. A powder, a granule, and a capsule

contg. the specific compd. I were described.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alleviation of side effects; prepn. of (hexahydroindolidinyl)heterocyclic compd. derivs. as inflammatory cytokine prodn. inhibitors and their medicinal use in combination with nonsteroidal antiinflammatory agents)
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)

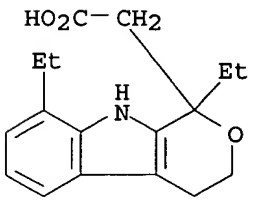


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:720729 CAPLUS
DOCUMENT NUMBER: 136:256719
TITLE: QSAR model for drug human oral bioavailability. [Erratum to document cited in CA133:159633]
AUTHOR(S): Yoshida, Fumitaka; Topliss, John G.
CORPORATE SOURCE: Division of Medicinal Chemistry College of Pharmacy, University of Michigan, Ann Arbor, MI, 48109-1065, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(24), 4723
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB On page 2578, Table 5, the correct footnote e is as follows: "e Weighting is 0.5, where the carbon .alpha. to the **carbonyl** is tertiary, or the **carbonyl** is attached to a ring with ortho substituents on each side, or the **carbonyl** can undergo intramol. hydrogen bonding with a nearby group.". On page 2580, in Table 6, under the "structural descriptors" column, the correct data for entries 96 and 133 is 7, 13 for both compds. Under the "drug" column, the correct spelling of the names for entries 83 and 107 are propranolol and chlorthalidone, resp.

IT **41340-25-4**, Etodolac
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); BIOL (Biological study)
(QSAR model for drug human oral bioavailability (Erratum))
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)

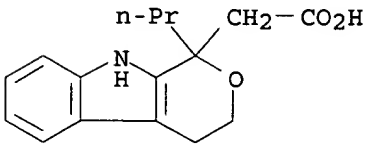


L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:31963 CAPLUS
DOCUMENT NUMBER: 126:101124
TITLE: A model for the active site of cyclooxygenase
AUTHOR(S): Kim, Yang Bae; Chung, Uoo Tae; Park, Il Yeong
CORPORATE SOURCE: College Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Yakche Hakhoechi (1996), 26(3), 155-168
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal
LANGUAGE: Korean

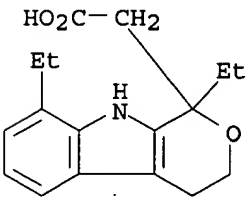
AB The active site of cyclooxygenase was modeled by complementary receptor-cavity mapping procedure using 3D structures of the non-steroidal anti-inflammatory drugs (NSAIDs). A total of 50 NSAIDs were chosen as data ligands which compete the same site on the enzyme. Partial at. charges were estd., and the energetic differences for various conformations were calcd. to meet the need for a most efficient overlapping of the probably-equiv. functional groups of the ligand mols. The structure activity relationships of the NSAIDs. if available, were fully considered throughout the modeling. The overall shape of the model obtained is similar to a boot-without-bottom. Most of inner surface of the cavity appeared as hydrophobic: two polar counterparts except the **carboxyl**-binding position were found. By this model, some clear explanations could be given on the exptl. observations which were not satisfactorily understood yet.

IT **36505-82-5**, Prodolic acid **41340-25-4**, Etodolac
114716-16-4, Pemedolac
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(model for active site of cyclooxygenase by mapping using 3D structures of non-steroidal anti-inflammatory drugs)

RN 36505-82-5 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,3,4,9-tetrahydro-1-propyl- (9CI) (CA INDEX NAME)



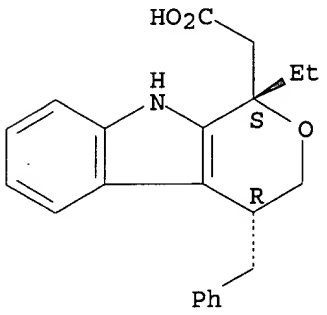
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



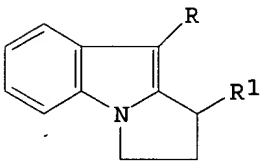
RN 114716-16-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1-ethyl-1,3,4,9-tetrahydro-4-(phenylmethyl)-, (1R,4S)-rel- (9CI) (CA INDEX NAME)

09/ 634,207

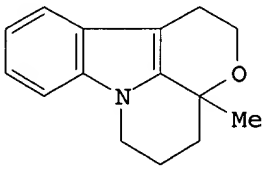
Relative stereochemistry.



L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:83880 CAPLUS
DOCUMENT NUMBER: 94:83880
TITLE: The reactions of four derivatives of pyrrolo[1,2-a]indole with arenesulfonyl azides
AUTHOR(S): Bahadur, Gulam A.; Bailey, A. Sydney; Scott, Peter W.; Vandrevala, Marazban H.
CORPORATE SOURCE: Dyson Perrins Lab., Univ. Oxford, Oxford, OX1 3QY, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1980), (12), 2870-7
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 94:83880
GI



I

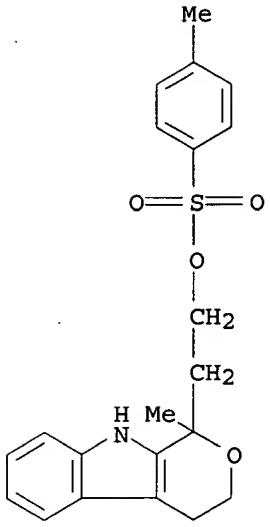


II

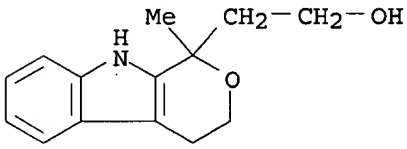
AB The reactions of the pyrroloindoles I (R = H, Me, R1 = H), the pyrrolocarbazole I [RR1 = (CH2)3], and the oxoazacyclopentafluorene II with arenesulfonyl azides were studied. E.g., I (R = R1 = H) with tolylsulfonyl azide (room temp., 60 h) gave a mixt. of the tolylsulfonylaminoindole (I; R = NHSO2C6H4Me-p, R1 = H) and 9,9'-azobis(2,3-dihydro-1H-pyrrolo[1,2-a]indole) (60 and 12%, resp.). The compn. of the product mixt. was dependent upon the azide structure and the solvent.

IT **76569-39-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of, tetrahydromethyloxaazacyclopentafluorene by)

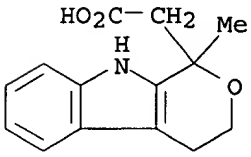
RN 76569-39-6 CAPLUS
CN Pyrano[3,4-b]indole-1-ethanol, 1,3,4,9-tetrahydro-1-methyl-, 4-methylbenzenesulfonate (ester) (9CI) (CA INDEX NAME)



IT **76569-38-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tolylsulfonylation of)
RN 76569-38-5 CAPLUS
CN Pyrano[3,4-b]indole-1-ethanol, 1,3,4,9-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



IT **41339-47-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(redn. of)
RN 41339-47-3 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,3,4,9-tetrahydro-1-methyl- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 13:20:13 ON 06 JAN 2004)

FILE 'REGISTRY' ENTERED AT 13:20:22 ON 06 JAN 2004
L1 STRUCTURE UPLOADED
L2 1256 S L1 FUL
L3 6 S MITOXANTRONE

09/ 634,207

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L4            40 S PREDNISONE
L5            13 S ESTRAMUSTINE
L6            17 S MELPHALAN
L7           155 S VINBLASTINE
L8             0 S BICAFUTAMIDE
L9             0 S BICAFLUTAMIDE
L10            1 S NILUTAMIDE
L11            5 S FLUTAMIDE

     FILE 'CAPLUS' ENTERED AT 13:26:29 ON 06 JAN 2004
L12          700 S L2
L13            4 S L12 AND (CARBONYL OR CARBOXYL OR SULFONYL OR SULPHONYL)

=> s l12 not l13
L14          696 L12 NOT L13

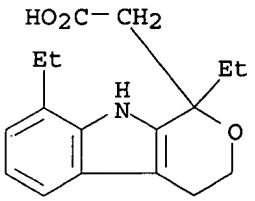
=> s l14 and (cancer? or leukemia or myeloma or prostate or hematopoietic or marrow or
'PPAR')
         215285 CANCER?
          80763 LEUKEMIA
          14898 MYELOMA
          34043 PROSTATE
          34096 HEMATOPOIETIC
          59703 MARROW
           4074 'PPAR'
L15           41 L14 AND (CANCER? OR LEUKEMIA OR MYELOMA OR PROSTATE OR HEMATOPOI
                 ETIC OR MARROW OR 'PPAR')

=> d l15 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 41 ANSWERS - CONTINUE? Y/(N):y

L15  ANSWER 1 OF 41  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:930958  CAPLUS
DOCUMENT NUMBER:          140:713
TITLE:                    Method of treating cervical cancer with an
                          inhibitor of cyclooxygenase-1 or with EP2 or EP4
                          receptor antagonists
INVENTOR(S):              Sales, Kurt Jason; Jabbour, Henry Nicolas; Katz, Arieh
PATENT ASSIGNEE(S):       UK
SOURCE:                   U.S. Pat. Appl. Publ., 32 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ----------------  ----  --------       ---------------  --------
     US 2003220266      A1   20031127       US 2002-284569   20021030
PRIORITY APPLN. INFO.:                   US 2001-340971P  P  20011030
AB   A method of treating a neoplastic condition of the cervix in a patient the
     method comprising administering to the patient an inhibitor of
     cyclooxygenase-1 (COX-1) and/or an EP2 and/or EP4 receptor antagonist.
     Overexpression of COX-1 in HeLa cells was assocd. with enhanced expression
     of the angiogenic factors: basic fibroblast growth factor (bFGF), vascular
     endothelial growth factor (VEGF), angiopoietin-1 (Ang-1) and
     angiopoietin-2 (Ang-2).  This upregulation of angiogenic factor expression
     was abolished by indomethacin.
IT   41340-25-4, Etodolac
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (COX-1 inhibitor; cervical cancer treatment with
        cyclooxygenase-1 inhibitors and/or with EP2 or EP4 receptor
```

antagonists)
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:855818 CAPLUS
DOCUMENT NUMBER: 139:345914
TITLE: Treating an autoimmune disease using a soluble CTLA4 molecule in combination with a DMARD or NSAID drug
INVENTOR(S): Cohen, Robert; Carr, Suzette; Hagerty, David; Peach, Robert J.; Becker, Jean-Claude
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 339 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088991	A1	20031030	WO 2003-US12356	20030418

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-373852P P 20020419
US 2002-407246P P 20020830

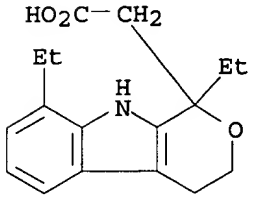
AB The present invention relates to compns. and methods for treating immune system diseases such as rheumatic disease, by administering to a subject sol. CTLA4 mols. that block endogenous B7 mols. from binding their ligands, alone, or in conjunction with other agents including disease modifying anti-rheumatic drugs (DMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs). The sol. CTLA4 mol. comprises the extracellular domain (residues 1-124) of full-length human CTLA4, which may be fused at the N-terminus with the signal peptide of oncostatin M and at the C-terminal end with an Ig C .gamma.1 domain. Single-site and double-site CTLA4 mutant sequences are also constructed, including L104E/A29Y-CTLA4/Ig, L104E/A29L-CTLA4/Ig, L104E/A29T-CTLA4/Ig, and L104E/A29W-CTLA4/Ig. CTLA4/Ig administered at 10 mg/kg (plus methotrexate) has superior efficacy in treatment of rheumatoid arthritis compared to placebo (plus metrotrexate) based on efficacy parameters of the American Collage of Rheumatol. Core Data Set and Response Definitions (ACR). Binding kinetics to CD86 and CD80, pharmacokinetics, and pharmacodynamics of C-reactive

protein, rheumatoid factor, interleukin-2 receptor, interleukin -6, and tumor necrosis factor .alpha. are provided.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-treatment with; treating an autoimmune disease using a sol. CTLA4 mol. in combination with a DMARD or NSAID drug)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

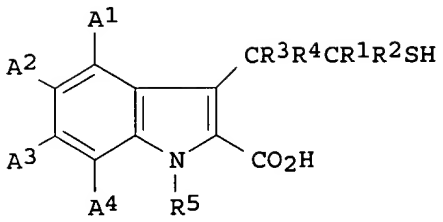
L15 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:551494 CAPLUS
DOCUMENT NUMBER: 139:101027
TITLE: Preparation of mercaptoethyl indolecarboxylic acids as NAALAdase inhibitors for treating and diagnosing glutamate abnormalities, neurological and other disorders
INVENTOR(S): Tsukamoto, Takashi; Grella, Brian; Majer, Pavel
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057670	A2	20030717	WO 2002-US37617	20021219
WO 2003057670	A3	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-342764P P 20011228
OTHER SOURCE(S): MARPAT 139:101027
GI



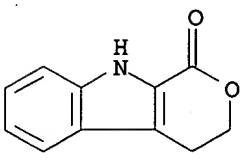
I

AB This invention relates to new indoles (shown as I; variables defined below; e.g. 3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid), pharmaceutical compns. and diagnostic kits comprising such compds., and methods of using such compds. for inhibiting NAALADase enzyme activity, detecting diseases where NAALAdase levels are altered, affecting neuronal activity, effecting TGF-.beta. activity, inhibiting angiogenesis, and treating glutamate abnormalities, neuropathy, pain, compulsive disorders, **prostate** diseases, **cancers** and glaucoma. IC50 values are tabulated for inhibition of NAALAdase by 12 examples of I. Many pharmacol. and therapeutic test results are reported for the following 6 compds. that are not covered by I: 2-[[(2,3,4,5,6-pentafluorobenzyl)hydroxyphosphinyl]methyl]pentanedioic acid, 2-(3-sulfanylpropyl)pentanedioic acid, 2-(phosphonomethyl)pentanedioic acid, 2-(2-sulfanylethyl)pentanedioic acid, 3-carboxy-.alpha.-(3-mercaptopropyl)benzenepropanoic acid and 3-carboxy-5-(1,1-dimethylethyl)-.alpha.-(3-mercaptopropyl)benzenepropanoic acid. For I: A1, A2, A3 and A4 = H, C1-C9 alkyl, C2-C9 alkenyl, C2-C9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C1-C9 alkoxy, C2-C9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, -COOR6, - COR6, -NR6R7, -SR6, -SOR6, -SO2R6, -SO2(OR6), -C(O)NR6R7, -C(O)NR6 (CH2)nCOOH, -NR6C(O)R7 or -(CH2)nCOOH, or any adjacent two of A1, A2, A3 and A4 form with the benzene ring a fused ring that is (un)satd., arom. or nonarom., and carbocyclic or heterocyclic, said heterocyclic ring contg. 1 or 2 O, N and/or S heteroatom(s); n is 1-3; R, R1, R2, R3, R4, R5, R6, R7 = H, carboxy, C1-C9 alkyl, C2-C9 alkenyl, C2-C9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy and fused ring (un)substituted with .gtoreq.1 substituent(s). Although the methods of prepn. are not claimed, 13 example prepns. are included.

IT **6250-88-0**, 4,9-Dihydro-3H-pyrano[3,4-b]indol-1-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of mercaptoethyl indolecarboxylic acids as NAALAdase inhibitors for treating and diagnosing glutamate abnormalities and neurol. and other disorders)

RN 6250-88-0 CAPLUS

CN Pyrano[3,4-b]indol-1(3H)-one, 4,9-dihydro- (9CI) (CA INDEX NAME)



L15 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:532133 CAPLUS
DOCUMENT NUMBER: 139:90470

09/ 634,207

TITLE: Topical application of .alpha.-DFMO and anti-inflammatory drug for treatment of actinic keratosis
INVENTOR(S): Alberts, David S.; Dorr, Robert T.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003129208	A1	20030710	US 2002-41236	20020107
WO 2003057172	A2	20030717	WO 2003-US375	20030107

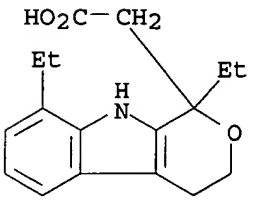
W: AU, NO
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2002-41236 A 20020107

AB Topical .alpha.-DFMO is mixed with a hydrophillic ointment base, along with at least 1 addnl. active drug, for treating actinic keratosis by topical application to human skin tissues. In one case, the topical steroid triamcinolone is combined with the .alpha.-DFMO. In a second case, the topical non-steroid anti-inflammatory diclofenac is combined with the .alpha.-DFMO. In a third instance, both triamcinolone and diclofenac are combined with the .alpha.-DFMO. In all such instances, topical application of such combinations inhibited squamous cell **cancer**, and the combined effect of such components, when selected in appropriate proportions, in inhibiting squamous cell **cancer** cells is significantly greater than the effectiveness of each such component by itself. The addn. of the topical steroid reduces alpha-DFMO induced inflammatory response in the skin. Addnl., the addn. of the topical steroid has been found to significantly enhance the effectiveness of topical alpha-DFMO in reducing squamous cell skin tumors implanted in immunodeficient mice. The combination of the topical steroid triamcinolone with topical alpha-DFMO has shown an unpredictable synergistic effect relative to redn. of squamous cell skin tumors.

IT **41340-25-4**, Etodolac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical application of .alpha.-DFMO and anti-inflammatory drug for treatment of actinic keratosis)

RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:404919 CAPLUS
DOCUMENT NUMBER: 139:207261
TITLE: Colon **cancer** cells with high invasive potential are susceptible to induction of apoptosis by

a selective COX-2 inhibitor

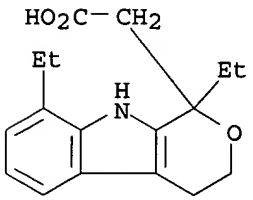
AUTHOR(S): Chen, Wei-Shone; Liu, Jin-Hwang; Wei, Sung-Jen; Liu, Jacqueline Ming; Hong, Chi-Yuan; Yang, Wen K.
CORPORATE SOURCE: Divisions of Colorectal Surgery, Veterans General Hospital-Taipei and National Yang-Ming University, Taiwan

SOURCE: Cancer Science (2003), 94(3), 253-258
CODEN: CSACCM; ISSN: 1347-9032
PUBLISHER: Japanese Cancer Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclooxygenase-2 (COX-2) expression has been shown to correlate with the invasiveness of colon **cancer** cells. To further investigate this pos. correlation and its possible therapeutic implications, a selective COX-2 inhibitor, etodolac, was tested on three variants of HT-29 colon **cancer** cell lines, HT-29/Inv1, HT-29/Inv2 and HT-29/Inv3, with graded increases of in vitro Matrigel invasive potential and COX-2 expression levels. HT-29 variants with higher invasive potential were found to be more sensitive to etodolac by in vitro growth inhibition assays, the estd. LD50 being 0.5 mM for highly invasive HT-29/Inv2 and HT-29/Inv3 cells, 0.6 mM for slightly less invasive HT-29/Inv1, and 1.8 mM for the parental HT-29. Treatment of the highly invasive HT-29/Inv2 and Inv3 variants with as little as 0.1 mM etodolac in the growth medium produced signs of apoptosis, as detected by DNA fragmentation and TUNEL (terminal deoxynucleotidyl transferase dUTP-biotin nick end labeling) assay. In vivo expts. in SCID mice showed that etolodac inhibited the growth of s.c. tumors induced by HT-29/Inv3 cells significantly more than those by the parental HT-29 cells. These results suggest that COX-2 inhibitors have a potential role in prevention of tumor invasion in colon **cancer** patients.

IT **41340-25-4**, Etodolac
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colon **cancer** cells with high invasive potential are susceptible to induction of apoptosis by a selective COX-2 inhibitor, etodolac)

RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:356241 CAPLUS
DOCUMENT NUMBER: 138:348694
TITLE: Use of antiinflammatory drugs in combination with antibiotics for reducing **prostate**-specific antigen (PSA) levels in men
INVENTOR(S): Fisch, Harry
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2

09/ 634,207

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037319	A1	20030508	WO 2002-US29713	20020919

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

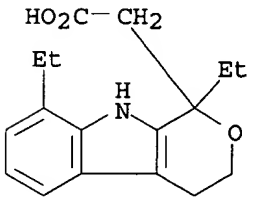
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-340909P P 20011029
US 2002-351157P P 20020123

AB A method for reducing an antigen indicator of **prostate cancer** and for reducing the need for biopsies in men suspected of having **prostate cancer** and a method for treating patients with elevated PSA levels. In one method, the level of an antigen indicator of **prostate cancer** is measured and for an above normal level of the antigen indicator, an effective amt. of an anti-inflammatory, or a combination of the anti-inflammatory and an antibiotic, is administered and the level of the antigen indicator is remeasured to det. if the level is normal or reduced, whereby a biopsy may not be indicated.

IT **41340-25-4**, Etodolac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of antiinflammatory drugs in combination with antibiotics for reducing **prostate**-specific antigen (PSA) levels in men)

RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:37511 CAPLUS
DOCUMENT NUMBER: 138:83095
TITLE: Induction of apoptosis in rheumatoid synovial fibroblasts by celecoxib, but not by other selective cyclooxygenase 2 inhibitors
AUTHOR(S): Kusunoki, Natsuko; Yamazaki, Ryuta; Kawai, Shinichi
CORPORATE SOURCE: St. Marianna University School of Medicine, Kawasaki, 216-8512, Japan
SOURCE: Arthritis & Rheumatism (2002), 46(12), 3159-3167

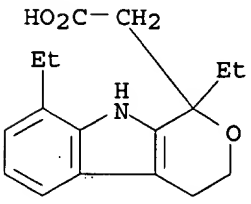
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Selective cyclooxygenase 2 (COX-2) inhibitors are now being used as antiinflammatory agents that cause fewer gastrointestinal complications, compared with other antiinflammatory drugs, in patients with rheumatoid arthritis (RA). This study was undertaken to investigate whether selective COX-2 inhibitors could induce apoptosis of RA synovial fibroblasts (RASFs). RASFs were exposed to selective COX-2 inhibitors, i.e., celecoxib, etodolac, meloxicam, nimesulide, N-[2-(cyclohexyloxyl)-4-nitrophenyl]-methanesulfonamide, and rofecoxib, under various conditions. Cell proliferation and cell viability were assessed by incorporation of 5-bromo-2'-deoxyuridine and by the 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium monosodium salt assay, resp. Apoptosis was detected by identifying DNA fragmentation. Activation of peroxisome proliferator-activated receptor .gamma. (**PPAR**.gamma.) was measured by the luciferase reporter gene assay with a **PPAR** response element-driven luciferase reporter plasmid and a **PPAR** .gamma. expression plasmid. Celecoxib strongly inhibited the proliferation of RASFs, whereas other selective COX-2 inhibitors had little or no effect. In addn., celecoxib reduced the viability of RASFs by induction of apoptosis, in a concn.-dependent manner. This action was abolished by addn. of caspase inhibitors. Interleukin-1.beta. had a weak enhancing effect on celecoxib-induced apoptosis in RASFs. In contrast, other selective COX-2 inhibitors at concns. up to 100 .mu.M did not induce apoptosis of RASFs. Indomethacin, a nonselective COX inhibitor, activated **PPAR**.gamma. transcription, while celecoxib did not. Celecoxib suppressed the proliferation of RASFs by COX-2-independent and **PPAR**.gamma.-independent induction of apoptosis. Although the mechanism involved remains unclear, celecoxib may have not only antiinflammatory activity, but also a disease-modifying effect on rheumatoid synovial proliferation.

IT **41340-25-4**, Etodolac
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of apoptosis in rheumatoid synovial fibroblasts by celecoxib, but not other selective COX-2 2 inhibitors in rheumatoid arthritis patients)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:946092 CAPLUS
DOCUMENT NUMBER: 138:11401
TITLE: Steroid hormone and nonsteroidal anti-inflammatory drug (NSAID) combinations for inducing tumor cell apoptosis
INVENTOR(S): Andrews, Peter; Djakiew, Daniel

09/ 634,207

PATENT ASSIGNEE(S): Georgetown University, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098403	A1	20021212	WO 2002-US17193	20020603

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

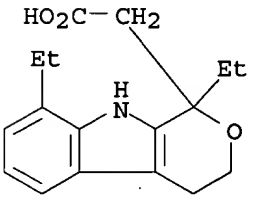
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-294583P P 20010601

AB A pharmaceutical compn. is described, having at least one nonsteroidal anti-inflammatory drug (NSAID), at least one steroid hormone, a pharmaceutically acceptable carrier, and optionally, one or more excipients, wherein the at least one NSAID and the at least one steroid hormone are present in amts. sufficient to induce tumor cell apoptosis. Also described is a method of inducing apoptosis of **cancer** cells in which therapeutically effective amts. of at least one NSAID and at least one steroid hormone are administered to a subject. The NSAID and steroid hormone may administered prophylactically to a subject having nonmeasurable tumor burden, or may be administered to a subject having a detectable tumor.

IT **41340-25-4**, Etodolac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroid hormone and nonsteroidal anti-inflammatory drug combination for inducing tumor cell apoptosis)

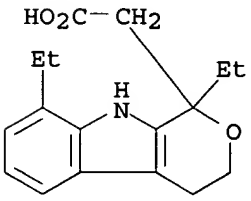
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:915121 CAPLUS
DOCUMENT NUMBER: 139:94907
TITLE: Effects of etodolac, a selective cyclooxygenase-2 inhibitor, on the expression of E-cadherin-catenin complexes in gastrointestinal cell lines
AUTHOR(S): Noda, Masao; Tatsumi, Yoichi; Tomizawa, Muneta; Takama, Takafumi; Mitsufuji, Shoji; Sugihara,

Hiroyuki; Kashima, Kei; Hattori, Takanori
CORPORATE SOURCE: Third Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto, 602-8566, Japan
SOURCE: Journal of Gastroenterology (2002), 37(11), 896-904
CODEN: JOGAET; ISSN: 0944-1174
PUBLISHER: Springer-Verlag Tokyo
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Recent studies have shown that cyclooxygenase-2 (COX-2) inhibitors may participate in the proliferation of **cancer** cells. Because the cadherin-catenin complex is not only a key component of the adherens junction but also has been suggested to regulate cell proliferation, modulation of these mols. may be a mechanism by which COX-2 activity affects cell proliferation. In this study, we evaluated the effect of a COX-2 inhibitor on the proliferation and expression of E-cadherin-complexes in gastrointestinal **cancer** cell lines. Methods: The gastrointestinal **cancer** cell lines Caco2, HT29, and MKN45 were grown for 24 h in the presence and absence of a selective COX-2 inhibitor, etodolac (10-5, 10-4, and 10-3 M). Cell proliferation was assessed by 3H-thymidine incorporation, and the expression of E-cadherin and catenins was assessed by Western blotting, Northern blotting, and immunofluorescence. Results: Etodolac induced a significant redn. in cell proliferation in Caco2 and MKN45 cells. E-cadherin expression was upregulated after stimulation with etodolac in Caco2 cells, whereas the expression of .alpha.-, .beta.-, .gamma.- and p120-catenins was not modified. The expression of E-cadherin mRNA was also upregulated in Caco2 cells, and was upregulated also in MKN45 cells, which did not express normal E-cadherin protein by the use of a mouse monoclonal antibody against human E-cadherin, HECD-1 antibody. Immunofluorescence revealed that the increased E-cadherin was localized at the cytoplasmic membrane. Conclusions: The inhibition of cell growth by etodolac in Caco-2 cells was assocd. with a dose-dependent upregulation and intense cytoplasmic localization of E-cadherin. No quant. change in catenin expression was found in this phenomenon. These findings suggest that the COX-2 inhibitor affects the transcription of E-cadherin, or that there may be some homeostatic link between the cell cycle and E-cadherin transcription.
IT **41340-25-4**, Etodolac
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(etodolac proliferation inhibition and E-cadherin-catenin complex expression upregulation in human gastrointestinal tumor cell lines)
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:754159 CAPLUS
DOCUMENT NUMBER: 137:263297
TITLE: Preparation of 2,7-diamino-5-heptenoic acid

09/ 634,207

derivatives for the treatment of **cancer**

INVENTOR(S): Manning, Pamela T.; Connor, Jane R.; Seibert, Karen; Rao, Chinthalapally V.; Reddy, Bandaru S.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 295 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076395	A2	20021003	WO 2002-US8938	20020321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003013702	A1	20030116	US 2001-961969	20010924

PRIORITY APPLN. INFO.: US 2001-278512P P 20010323
US 2001-961969 A 20010924

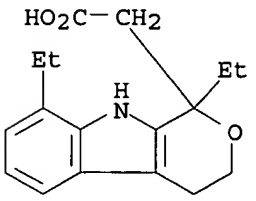
OTHER SOURCE(S): MARPAT 137:263297

AB Agents and methods for chemoprevention and treatment of neoplasia are described, the agents including a selective inhibitor of inducible nitric oxide synthase and a combination of a selective inhibitor of inducible nitric oxide synthase and an inhibitor of cyclooxygenase-2 in a pharmaceutical compn. 2,7-Diamino-5-heptenoic acid derivs. R7N:CMeNHCH2CR1:CR2CH2CH2CH(NH2)C(O)J [R1, R2 = H, halo, alkyl, haloalkyl (at least one of R1 or R2 contains halogen); R7 = H, OH; J = OH, alkoxy, NR3R4, where R3 = H, alkyl, alkenyl, alkynyl and R4 = H, (un)substituted heterocyclyl] or their pharmaceutically-acceptable salts are among the compds. claimed. Thus, (2S,5E)-2-amino-6-fluoro-7-[(1-iminoethyl)amino]-5-heptenoic acid dihydrochloride was prepd. by a multistep procedure starting from L-glutamic acid and showed IC50 values 0.36, 68, 3.6, and 0.1 .mu.M in hiNOS, hecNOS, hncNOS, and human cartilage assays, resp.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of diaminoheptenoic acid derivs. for treatment of **cancer**)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:611609 CAPLUS

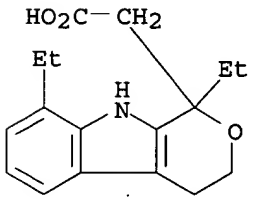
DOCUMENT NUMBER: 137:335864

09/ 634,207

TITLE: Size-dependent expression of cyclooxygenase-2 in sporadic colorectal adenomas relative to adenomas in patients with familial adenomatous polyposis
AUTHOR(S): Azumaya, Masaki; Kobayashi, Masaaki; Ajioka, Yoichi; Honma, Terasu; Suzuki, Yutaka; Takeuchi, Manabu; Narisawa, Rintarou; Asakura, Hitoshi
CORPORATE SOURCE: Third Department of Internal Medicine, Niigata University School of Medicine, Niigata, Japan
SOURCE: Pathology International (2002), 52(4), 272-276
CODEN: PITEES; ISSN: 1320-5463
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several studies have indicated that administration of non-steroidal anti-inflammatory drugs (NSAID) to patients with familial adenomatous polyposis (FAP) results in a regression of colorectal adenomas through inhibition of cyclooxygenase-2 (COX-2). It is thought that sporadic colorectal adenomas might also be useful targets for the chemoprevention of colorectal **cancer**, but a marked effect of NSAID on the regression of sporadic adenomas has not been obsd. We investigated the immunohistochem. expression of COX-2 in sporadic tubular adenomas (n = 100) from 63 patients and in tubular adenomas (n = 121) from 12 patients with FAP, in order to det. if chemoprevention might be more successful in sporadic adenomas once they have reached a certain size. COX-2 scores were significantly lower (P<0.0001) in small (< 5 mm in diam.) adenomas than in large (.gtoreq. 5 mm) adenomas. This was obsd. in both sporadic cases and in cases involving patients with FAP. With regard to small (< 5 mm) adenomas, significantly higher (P = 0.02) COX-2 scores were obtained in adenomas resulting from FAP than sporadic adenomas. The variation in COX-2 expression obsd. among sporadic adenomas of different sizes should be taken into account when making decisions regarding attempts at chemoprevention using NSAID. Sporadic adenomas 5 mm or larger with upregulated COX-2 expression are potentially useful targets for the anti-proliferative effects of NSAID.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(size-dependent expression of cyclooxygenase-2 in sporadic colorectal adenomas relative to adenomas in patients with familial adenomatous polyposis)
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

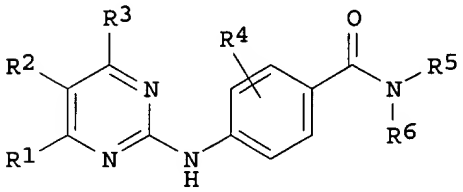
L15 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:449662 CAPLUS
DOCUMENT NUMBER: 137:33310
TITLE: Preparation of anilinopyrimidines as IKK inhibitors
INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.

09/ 634,207

PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046171	A2	20020613	WO 2001-US46403	20011205
WO 2002046171	A3	20030123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003203926	A1	20031030	US 2001-4642	20011204
AU 2002020195	A5	20020618	AU 2002-20195	20011205
EP 1349841	A2	20031008	EP 2001-999564	20011205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-251816P P 20001206
WO 2001-US46403 W 20011205
OTHER SOURCE(S): MARPAT 137:33310
GI

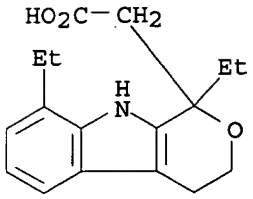


I

AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of IKK, particularly IKK-2, were prepd. E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of .ltoreq. 1 .mu.M in the IKK-2 enzyme assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to IKK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. contg. one or more compds. of the above compds.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory agent; prepn. of anilinopyrimidines as IKK inhibitors)

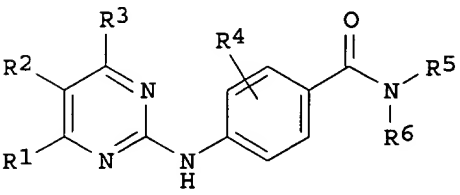
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:449661 CAPLUS
DOCUMENT NUMBER: 137:33309
TITLE: Preparation of anilinopyrimidines as JNK pathway inhibitors
INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.
PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046170	A2	20020613	WO 2001-US46402	20011205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003220330	A1	20031127	US 2001-4645	20011204
AU 2002027214	A5	20020618	AU 2002-27214	20011205
EP 1349840	A2	20031008	EP 2001-996103	20011205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-251904P P 20001206
WO 2001-US46402 W 20011205
OTHER SOURCE(S): MARPAT 137:33309
GI



I

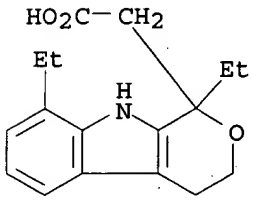
AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of the JNK pathway, were

prepd. E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of .ltoreq. 10 .mu.M in the JNK2 assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to inhibition of the JNK pathway. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. contg. one or more compds. of the above compds.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory agent; prepn. of anilinopyrimidines as JNK pathway inhibitors)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:276519 CAPLUS
DOCUMENT NUMBER: 136:310188
TITLE: Treatment of **cancer** with a **prostate** specific antigen (PSA) conjugate and an NSAID compound
INVENTOR(S): Heimbrook, David C.; Yao, Siu-long
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 129 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002042375	A1	20020411	US 2001-896245	20010629

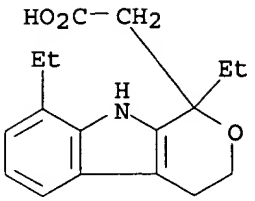
PRIORITY APPLN. INFO.: US 2000-216217P P 20000705
OTHER SOURCE(S): MARPAT 136:310188

AB The invention relates to methods of treating **cancer** using a combination of a compd. which is a PSA conjugate and a nonsteroidal antiinflammatory agent (NSAID) and to methods of prepg. such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg = cyclohexylglycine) and COX-2 inhibitor 3-phenyl-4-[4-(4-methylsulfonyl)phenyl]-2(5H)furanone is an example of an NSAID compd. (syntheses given).

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of **cancer** with **prostate** specific antigen (PSA) conjugate and NSAID compd.)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:122955 CAPLUS
DOCUMENT NUMBER: 136:161347
TITLE: Indole compounds useful for the treatment of **cancer**
INVENTOR(S): Carson, Dennis A.; Leoni, Lorenzo M.; Cottam, Howard B.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012188	A2	20020214	WO 2001-US24978	20010809
WO 2002012188	A3	20021003		
WO 2002012188	B1	20030320		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001083224	A5	20020218	AU 2001-83224	20010809
EP 1307459	A2	20030507	EP 2001-962006	20010809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-634207 A 20000809
WO 2001-US24978 W 20010809
OTHER SOURCE(S): MARPAT 136:161347

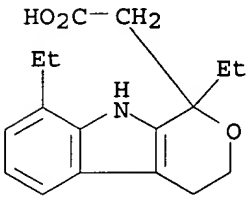
AB The present invention provides novel indole derivs. useful to inhibit **cancer** or sensitize **cancer** cells to chemotherapeutic agents, radiation or other anti-**cancer** treatments. The present compds. can be used to treat a mammal afflicted with **cancer**, such as a human **cancer** patient, and are preferably administered in conjunction with a chemotherapeutic agent, such as an alkylating agent or an antiandrogen, radiation and/or other anticancer therapy. The present compds. are effective against **hematopoietic cancers**, such as leukemias and **cancers** of the bone **marrow**, including chronic lymphocytic **leukemia** (CLL) and multiple **myeloma** (MM). The present compds. were unexpectedly effective against **cancer** cells that express high levels of the nuclear hormone receptor, peroxisome proliferator activated receptor-.gamma., **PPAR**-.gamma., and/or high levels of the antiapoptotic proteins, Mcl-1 and/or Bag-1. Compds. that activate **PPAR**-.gamma. prodn. can reduce the level of expression of the

androgen receptor known to be overexpressed in hormone-resistant **prostate cancer**. Therefore, the present compds. can enhance the efficacy of conventional antiandrogen therapy, and can act to inhibit the spread of **prostate cancer**.

IT **41340-25-4**, Etodolac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indole compds. useful for treatment of **cancer** and synergistic combinations)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:89826 CAPLUS
DOCUMENT NUMBER: 136:129055
TITLE: Method using a cyclooxygenase 2 (COX-2) inhibitor for treatment of an immunodeficiency condition
INVENTOR(S): Tasken, Kjetil; Moutschen, Michel; Rahmouni-Piette, Souad; Aandahl, Einar Martin; Aukrust, Pal; Froland, Stig S.; Johansson, Christian Carl; Hansson, Vidar; Klaveness, Jo
PATENT ASSIGNEE(S): Lauras AS, Norway; Jones, Elizabeth Louise
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007721	A2	20020131	WO 2001-GB3284	20010720
WO 2002007721	A3	20020418		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1303265	A2	20030423	EP 2001-949787	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003000276	A	20030318	NO 2003-276	20030120

PRIORITY APPLN. INFO.: GB 2000-17908 A 20000720
GB 2001-9648 A 20010419
WO 2001-GB3284 W 20010720

OTHER SOURCE(S): MARPAT 136:129055

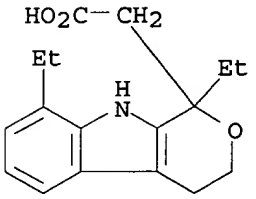
09/ 634,207

AB The invention provides a method of treating or preventing a disorder typified by an immunodeficiency (e.g. HIV), wherein the patient is administered a COX-2 inhibitor or deriv. or pharmaceutically acceptable salt thereof, preferably diisopropylfluorophosphate, L-745337, rofecoxib, NS 398, SC 58125, etodolac, meloxicam, celecoxib or nimesulide, as well as compns. and products contg. the same or use of the same in prepg. medicaments and for treatment.

IT **41340-25-4**, Etodolac
RL: AGR (Agricultural use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor for immunodeficiency condition treatment)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:693651 CAPLUS
DOCUMENT NUMBER: 135:240908
TITLE: Assay for agents that induce chemokinesis
INVENTOR(S): Carson, Dennis A.; Leoni, Lorenzo M.; Cottam, Howard B.
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001069240	A1	20010920	WO 2001-US8581	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002010125	A1	20020124	US 2001-810010	20010316
EP 1269183	A1	20030102	EP 2001-920474	20010316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527603	T2	20030916	JP 2001-568069	20010316

PRIORITY APPLN. INFO.: US 2000-189976P P 20000316
WO 2001-US8581 W 20010316

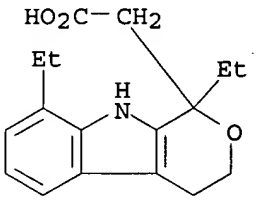
AB The present invention provides methods for identifying compds. that can induce cellular chemokinesis. According to the present invention, chemokinesis interferes with immune and inflammatory responses by increasing cell movements and altering cell migration patterns.

Surprisingly, compds. isolated according to the present invention can interfere with the spread of malignant cells through the body, reduce inflammatory responses and can cause leukocytes to be retained in lymph nodes, the spleen and other organs of the reticulo-endothelial system. Several methods are contemplated by the present invention for identifying compds. which can induce chemokinesis. In one embodiment the method involves contacting a population of target cells with a test compd. and observing whether the target cells produce a chemotactic mol.; wherein the target cell has a cognate receptor for the chemotactic mol. In another embodiment, the method involves contacting a population of target cells with a test compd. and observing whether the targets cells homotypically aggregate. In yet another embodiment, the method involves contacting a population of target cells with a test compd. and observing whether actin filaments in the target cells form stress fibers.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(assay for chemokinesis-inducing agents and agent use for interference with immune and inflammatory responses for inhibition of **cancer** and transplant rejection and autoimmunity and other diseases)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:605491 CAPLUS

DOCUMENT NUMBER: 136:303669

TITLE: Induction of apoptosis by cyclooxygenase-2 inhibitors in **prostate cancer** cell lines

AUTHOR(S): Kamijo, Toshiyuki; Sato, Toshikazu; Nagatomi, Yutaka; Kitamura, Tadaichi

CORPORATE SOURCE: Department of Urology, Faculty of Medicine, University of Tokyo, Tokyo, 113-8655, Japan

SOURCE: International Journal of Urology (2001), 8(7), S35-S39
CODEN: IJURF3; ISSN: 0919-8172

PUBLISHER: Blackwell Science Asia Pty Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

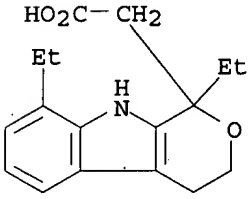
AB Prostaglandins are thought to play an important role in the proliferation of **prostate cancer** and are highly expressed in **prostate cancer** tissue. Cyclooxygenase-2 (COX-2), or prostaglandin endoperoxide synthase, is a key enzyme in the conversion of arachidonic acid into prostaglandin. In several **cancers**, COX-2 contributes to the proliferation and metastasis of **cancer** cells. To assess the role of COX-2 in **prostate cancer**, we investigated whether the inhibition of COX-2 affected the proliferation of **prostate cancer** cells. The human **prostate cancer** cell lines, LNCaP and PC 3, and a normal **prostate** stromal cell line (PrSC) were treated with COX-2 inhibitors NS 398 and

Etodolac. The proliferation rate of the cell lines was examd. using 3(4,5-dimethylethiazoly 1-2-) 2,5-di-Ph tetrazolium bromide (MTT) assays. A DNA fragmentation assay was also used for proof of apoptosis. COX-2 inhibitors could suppress the proliferation of LNCaP and PC 3 cells. In contrast, PrSC was not affected by COX-2 inhibitors. These suppressive effects occurred in a time-and dose-dependent manner. One of mechanisms responsible for cell death was apoptosis. COX-2 seems to play a significant role in the progression of **prostate cancer** . COX-2 may be a therapeutic target for **prostate cancer** . Since COX-2 inhibitors suppress proliferation and induce apoptosis in **prostate cancer** cells, and have no effect in normal **prostate** stromal cells, COX-2 inhibitors will be useful for the treatment of **prostate cancer**.

IT **41340-25-4**, Etodolac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of apoptosis by cyclooxygenase-2 inhibitors (NS 398 and Etodolac) in **prostate cancer** cell lines)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:466147 CAPLUS

DOCUMENT NUMBER: 136:35637

TITLE: Involvement of cyclooxygenase-2 in hyperplastic gastritis induced by Helicobacter pylori infection in C57BL/6 mice

AUTHOR(S): Xiao, F.; Furuta, T.; Takashima, M.; Shirai, N.; Hanai, H.

CORPORATE SOURCE: First Department of Medicine, Hamamatsu University School of Medicine, Hamamatsu, 431-3192, Japan

SOURCE: Alimentary Pharmacology and Therapeutics (2001), 15(6), 875-886
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

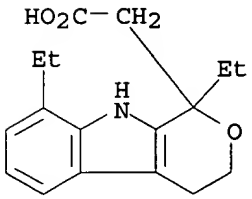
AB Background and aims: The hyperplastic changes obsd. in Helicobacter pylori-assocd. gastritis have been considered to increase the risk of gastric **cancer**. The aim of this study was to det. whether cyclooxygenase-2 is involved in the hyperplastic changes in mice infected with H. pylori. Methods: Seven-week-old. male C57BL/6 mice (n = 40) were inoculated with the Sydney strain of H. pylori. Control mice (n = 40) were treated with vehicle only. Half of the infected and control mice were fed an exptl. diet contg. etodolac (10 mg/kg/day) from 1 wk after inoculation until the end of the expt. The thickness of gastric pits, COX-2 mRNA and protein levels, and prostaglandin E2 (PGE2) levels in the gastric mucosa were detd. before and 12, and 24 wk after inoculation. Results: The thickness of gastric pits, COX-2 mRNA and protein levels, and

PGE2 levels were significantly increased at 24 wk after inoculation of H. pylori compared with the control groups. Treatment with etodolac resulted in significant decreases in PGE2 prodn. and in the thickness of gastric pits in the infected groups at 24 wk after inoculation. Conclusions: Our findings suggest that COX-2 is involved in the development of hyperplastic gastritis caused by H. pylori infection via the prodn. of PGE2.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 role in hyperplastic gastritis induced by Helicobacter pylori infection in C57BL/6 mice)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:355060 CAPLUS
DOCUMENT NUMBER: 134:357577
TITLE: Local delivery of non-steroidal anti-inflammatory drugs (NSAIDs) to the colon as a treatment for colonic polyps
INVENTOR(S): Lerner, E. Itzhak; Flashner, Moshe; Penhasi, Adel
PATENT ASSIGNEE(S): Perio Products Ltd., Israel
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,840,332.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6231888	B1	20010515	US 1998-190127	19981112
US 5840332	A	19981124	US 1996-588247	19960118
ZA 9700405	A	19970730	ZA 1997-405	19970117
CN 1208343	A	19990217	CN 1997-191743	19970117
WO 2000028974	A1	20000525	WO 1999-IL607	19991112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1131058	A1	20010912	EP 1999-972097	19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-588247 A2 19960118
US 1998-190127 A 19981112

09/ 634,207

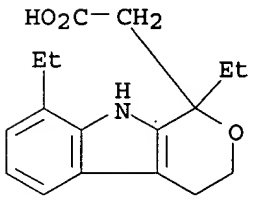
WO 1999-IL607 W 19991112

AB A compn. or drug delivery device for localized release and/or preferential metab. of drugs, esp. an NSAID, in the colon for the treatment of polyp and colon **cancer** is described. NSAID agents are inhibitors of COX-1 or COX-2. The dose of NSAID agent is 2-500 mg/day for 1-12 mo in single or divided doses. For example, colon delivery system (CDS) formulations of sulindac prevented the release of sulindac in the upper gastrointestinal tract and deliver the sulindac to the colon. It has been further shown that the sulindac that is delivered to the colon is metabolized in the colon to its major metabolites, sulindac sulfide and sulindac sulfone. This metab. shows a preference for the sulindac sulfide over the sulindac sulfone. Some of the sulindac sulfone (perhaps most) is formed from the sulindac sulfide after absorption into the blood. It is inferred that the local concn. of sulindac sulfide is relatively high in the colon before absorption into the blood. Sulindac sulfide is the more active metabolite in processes that require inhibition of prostaglandin and esp. in processes dependent on COX-2 inhibition. The CDS formulations described are a more efficient way of delivering the sulindac sulfide metabolite to the colon for treatment of colonic diseases such as polyps or colon **cancer** than conventional delivery.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local delivery of NSAIDs to colon as treatment for colon **cancer** and polyps)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 132 THERE ARE 132 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:155053 CAPLUS

DOCUMENT NUMBER: 135:146955

TITLE: Tumor invasiveness and liver metastasis of colon **cancer** cells correlated with cyclooxygenase-2 (COX-2) expression and inhibited by a COX-2-selective inhibitor, etodolac

AUTHOR(S): Chen, Wei-Shone; Wei, Sung-Jen; Liu, Jacqueline Ming; Hsiao, Michael; Jen, Kou-Lin; Yang, Wen K.

CORPORATE SOURCE: Veterans General Hospital-Taipei, National Yang-Ming University, Taipei, Taiwan

SOURCE: International Journal of Cancer (2001), 91(6), 894-899
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

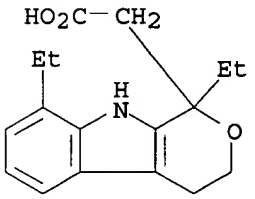
AB Non-steroidal anti-inflammatory drugs (NSAIDs) have been reported to reduce the risk and mortality of colorectal **cancer** (CRC). Although the exact mechanisms remain unclear, the inhibition of

cyclooxygenase (COX) by NSAIDs appears to abort, if not prevent, CRC carcinogenesis or metastatic tumor progression. The aim of our study was to investigate the assocn. between COX-2 expression and CRC tumor cell invasiveness. The differences in immunoblot-detectable COX-2 protein contents in primary CRCs, metastatic hepatic lesions and corresponding normal mucosa from the same individual were evaluated in 17 patients. Three different colon **cancer** cell lines, SW620, Lovo, HT-29 and a metastatic variant of HT-29, HT-29/Inv3, were employed to evaluate COX-2 expression and prostaglandin E2 (PGE2) prodn. in relation to their invasive abilities in vitro. The effects of a COX-2-selective inhibitor, etodolac, on cell proliferation and invasive activity were also detd. The results showed that 15 of 17 (88%) metastatic CRC cells from the liver and 14 of 17 (82%) primary CRC tissue exhibited much higher levels of COX-2 than corresponding adjacent normal mucosa from the same patient. Among those patients with relatively high COX-2 expression in the primary tumors, almost all exhibited even higher levels of COX-2 in their hepatic metastases. Among the 4 colon **cancer** cell lines, HT-29/Inv3 manifested the highest COX-2 expression, PGE2 prodn. and in vitro invasive activity. The selective COX-2 inhibitor, etodolac, could esp. exert cytotoxicity and markedly suppress the invasive property and PGE2 prodn., although not the COX-2 protein level, in HT-29/Inv3 cells. Our results imply that COX-2 expression may be assocd. with the invasive and metastatic properties of CRC tumor cells.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor invasiveness and liver metastasis of colon **cancer** cells correlated with cyclooxygenase-2 (COX-2) expression and inhibited by a COX-2-selective inhibitor, etodolac)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:137057 CAPLUS
DOCUMENT NUMBER: 134:173040
TITLE: NSAID- and EGFR kinase inhibitor-containing composition for the treatment or inhibition of colonic polyps and colorectal **cancer**
INVENTOR(S): Frost, Philip; DiScafani-Marro, Carolyn Mary
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001012227	A1	20010222	WO 2000-US21021	20000802	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
BR 2000013219	A	20020423	BR 2000-13219	20000802	
EP 1202746	A1	20020508	EP 2000-950930	20000802	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003507342	T2	20030225	JP 2001-516570	20000802	
US 6432979	B1	20020813	US 2000-634787	20000809	
NO 2002000663	A	20020409	NO 2002-663	20020211	
PRIORITY APPLN. INFO.:			US 1999-373261	A 19990812	
			US 1999-198212P	P 19990812	
			WO 2000-US21021	W 20000802	

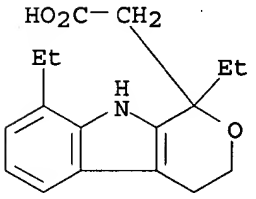
OTHER SOURCE(S): MARPAT 134:173040

AB A method is provided for treating or inhibiting colonic polyps or colorectal **cancer** in a mammal in need thereof which comprises administering an NSAID and an EGFR kinase inhibitor. A NSAID, sulindac, and an EGFR kinase inhibitor, N-[4-((3-bromophenyl)amino)6-quinazolinyl]-2-butynamide, showed synergistic activity in redn. of intestinal polyps in an animal model.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAID- and EGFR kinase inhibitor-contg. compn. for treatment of colon polyps and colorectal **cancer**)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:111692 CAPLUS

DOCUMENT NUMBER: 134:125692

TITLE: Inhibitory effects of clarithromycin and/or etodolac on lung carcinogenesis initiated by N-nitrosobis(2-hydroxypropyl)amine in rats

AUTHOR(S): Murakawa, Koichi

CORPORATE SOURCE: Dep. Oncnol. Pathol., Cancer Cent., Nara Med. Univ., Japan

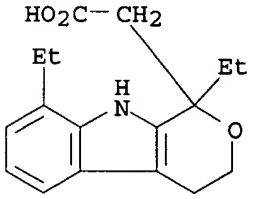
SOURCE: Journal of Nara Medical Association (2000), 51(6), 407-418
CODEN: JNMAFJ

PUBLISHER: Nara Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The inhibitory effects of antibiotics and a cyclooxygenase (COX)-2 inhibitor on lung carcinogenesis in rats initiated with N-nitrosobis(2-hydroxypropyl)amine (BHP) were investigated. Male Wistar rats were given tap water without BHP or tap water contg. 2000 ppm BHP with a basal diet for 12 wk followed by the basal diet or the diet contg. test compds. for 8 wk. Rats received basal diet or diets contg. 0.02% clarithromycin (CAM), 0.015% etodolac, 0.02% CAM plus 0.015% etodolac, resp. The incidences of lung lesions were not different but the nos. of lesions including adenocarcinoma (AC), squamous cell carcinoma (SCC), and adenosquamous carcinoma (ASCC) decreased in rats given CAM, etodolac or CAM plus etodolac as compared with those in rats given no drugs. In the lungs of rats which received the drugs, the suppression of chronic inflammation in the alveolar spaces and walls was evident. The labeling index of proliferating cell nuclear antigen (PCNA) decreased in alveolar hyperplasia (AH) in the lungs of rats which received CAM, etodolac, and CAM plus etodolac; however, 8-hydroxydeoxyguanosine (8-OHdG) generation studied by immunohistochem. did not differ between the lungs of rats with or without the administration of drugs. The results indicate that the suppression of chronic inflammation may inhibit the progression of lung carcinogenesis by BHP in rats and possibly provide a chemotherapeutic strategy for controlling advanced lung **cancer**.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitory effect of clarithromycin and etodolac on lung carcinogenesis initiated by N-nitrosobis(2-hydroxypropyl)amine in rat)

RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:103777 CAPLUS
DOCUMENT NUMBER: 135:116703
TITLE: Increased expression of cyclooxygenase-2 in human pancreatic neoplasms and potential for chemoprevention by cyclooxygenase inhibitors
AUTHOR(S): Kokawa, Atsushi; Kondo, Hitoshi; Gotoda, Takuji; Ono, Hiroyuki; Saito, Daizo; Nakadaira, Saori; Kosuge, Tomoo; Yoshida, Shigeaki
CORPORATE SOURCE: Department of Gastrointestinal Oncology and Endoscopy, National Cancer Center Hospital, Tokyo, 104-0045, Japan
SOURCE: Cancer (New York, NY, United States) (2001), 91(2), 333-338
CODEN: CANCAR; ISSN: 0008-543X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

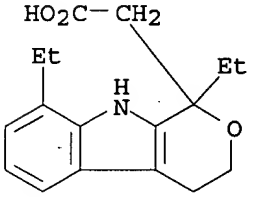
09/ 634,207

AB Cyclooxygenase-2 (COX-2) is thought to be linked to carcinogenesis; however, very little is known about its expression in pancreatic neoplasms. The authors studied the expression of COX-2 in human pancreatic neoplasms and investigated the effect of COX inhibitors on the growth of human pancreatic carcinoma cells. Expression of COX-2 protein was immunohistochem. examd. in 42 human pancreatic duct cell carcinomas (PDCs) and in 29 intraductal papillary mucinous tumors (IPMTs [adenomas, 19; carcinomas, 10]) of the pancreas that were resected surgically at the National **Cancer** Center Hospital in Tokyo. The growth of four human pancreatic carcinoma cell lines also was evaluated in the presence of COX inhibitors. Marked COX-2 expression was obsd. in 57% (24 of 42) of PDCs, in 58% (11 of 19) of adenomas, and in 70% (7 of 10) of adenocarcinomas of IPMTs. However, there was no correlation between COX-2 expression and clinicopathol. indexes of the patients. All four pancreatic **cancer** cell lines expressed COX-2 protein weakly or strongly, and the inhibitory effect of aspirin on cell growth was correlated with the expression of COX-2. COX-2 was expressed in adenomas of IPMTs as well as in carcinomas and might have played a role in the development of pancreatic tumors. In this study, COX inhibitors, as nonsteroidal anti-inflammatory drugs, were shown to be possible preventive agents against pancreatic neoplasms.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased expression of cyclooxygenase-2 in human pancreatic neoplasms and potential for chemoprevention by cyclooxygenase inhibitors)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:78184 CAPLUS
DOCUMENT NUMBER: 134:110452
TITLE: Use of etodolac in the treatment of **cancer**
INVENTOR(S): Carson, Dennis A.; Cottam, Howard B.; Adachi, Souchi; Leoni, Lorenzo M.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001006990	A2	20010201	WO 2000-US40370	20000713
WO 2001006990	A3	20010426		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6545034	B1	20030408	US 1999-360020	19990723
EP 1204412	A2	20020515	EP 2000-961986	20000713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003529542	T2	20031007	JP 2001-511882	20000713
NO 2002000358	A	20020321	NO 2002-358	20020123
US 2003078293	A1	20030424	US 2002-236221	20020905

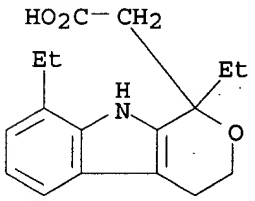
PRIORITY APPLN. INFO.: US 1999-360020 A 19990723
US 2000-589476 A 20000607
WO 2000-US40370 W 20000713

AB A method of treating **cancer**, e.g. multiple **myeloma** (MM), is provided comprising administering an amt. of etodolac to a subject afflicted with MM that is effective to selectively reduce the viability of and/or sensitize the **cancer** cells to an anti-**cancer** agent.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(etodolac in the treatment of **cancer**)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:31357 CAPLUS
DOCUMENT NUMBER: 134:80814
TITLE: Cyclooxygenase inhibitor and HMG-CoA reductase inhibitor as medicinal compositions for treating colorectal **cancer**
INVENTOR(S): Tanida, Norifumi; Goto, Takeshi; Tomizawa, Naoko
PATENT ASSIGNEE(S): Hisamitsu Pharmaceutical Co., Inc., Japan
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002014	A1	20010111	WO 2000-JP4327	20000630
W: AU, CA, CN, ID, JP, KR, US, VN				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				

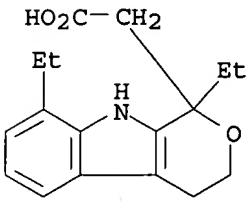
PT, SE
EP 1197228 A1 20020417 EP 2000-942407 20000630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
US 6620834 B1 20030916 US 2002-19469 20020415
PRIORITY APPLN. INFO.: JP 1999-188408 A 19990702
WO 2000-JP4327 W 20000630

AB Medicinal compns. for colorectal **cancer** to be administered to the large intestine by taking advantage of prepns. disintegrating in the large intestine, characterized by contg. a cyclooxygenase inhibitor and an HMG-CoA reductase inhibitor. These compns. are appropriate for inhibiting the postoperative liver metastasis and recurrence of colorectal **cancer**.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase inhibitor and HMG-CoA reductase inhibitor as medicinal compns. for treating colorectal **cancer**)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:903389 CAPLUS
DOCUMENT NUMBER: 135:55583
TITLE: Sulindac and a cyclooxygenase-2 inhibitor, etodolac, increase APC mRNA in the colon of rats treated with azoxymethane
AUTHOR(S): Kishimoto, Y.; Takata, N.; Jinnai, T.; Morisawa, T.; Shiota, G.; Kawasaki, H.; Hasegawa, J.
CORPORATE SOURCE: Department of Clinical Pharmacology, Faculty of Medicine, Tottori University, Yonago, 683-8503, Japan
SOURCE: Gut (2000), 47(6), 812-819
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

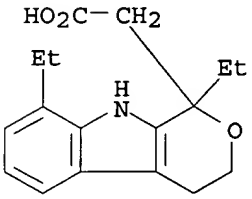
AB Non-steroidal anti-inflammatory drugs (NSAIDs) were reported to protect against the development of colon **cancer**. However, the mechanism(s) by which NSAIDs exert their effects is not clear. The aim of this study was to examine the effects of NSAIDs on mRNA expression of tumor suppressor adenomatous polyposis coli (APC) gene in rat colon mucosa. Starting at 6 wk of age, 3 groups of rats (groups 1, 2, and 3) were treated with azoxymethane (AOM), a colon specific carcinogen, and another 3 groups (groups 4, 5, and 6) were not given AOM. Groups 2 and 3 were given 10 mg/kg of sulindac or etodolac, resp., 3 times weekly during the expt. Groups 4 and 5 were also given sulindac or etodolac, resp., in the same manner as in groups 2 and 3. Groups 6 (untreated control) was not given any agent (AOM or NSAIDs). At 10 wk of age, preneoplastic

lesions (aberrant crypt foci (ACF)) induced by AOM in the colon were counted, and the level of expression of APC mRNA in the colonic mucosa was estd. by the reverse transcription-competitive polymerase chain reaction method and northern blot anal. Mean occurrence of ACF in rats in groups 2 and 3 was reduced to approx. 50% of that in group 1. The level of APC mRNA expression in group 1 (AOM alone) was lower than that in group 6 (untreated control); however, levels of APC mRNA expression in groups 2, 3, 4, and 5, to which NSAIDs had been administered, were increased compared with levels in groups 1 and 6. Both sulindac and etodolac reduced the occurrence of ACF and induced an increase in APC mRNA in rat colon mucosa.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAIDs on aberrant crypt foci formation and APC mRNA level)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:829877 CAPLUS

DOCUMENT NUMBER: 134:216922

TITLE: Inhibition of Epstein-Barr virus early antigen activation promoted by 12-O-tetradecanoylphorbol-13-acetate by the non-steroidal anti-inflammatory drugs

AUTHOR(S): Kapadia, G. J.; Azuine, M. A.; Takayasu, J.; Konoshima, T.; Takasaki, M.; Nishino, H.; Tokuda, H.

CORPORATE SOURCE: School of Pharmacy, Department of Pharmaceutical Sciences, Laboratory of Natural Drug Products, Howard University, Washington, DC, 20059, USA

SOURCE: Cancer Letters (Shannon, Ireland) (2000), 161(2), 221-229
CODEN: CALEDQ; ISSN: 0304-3835

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

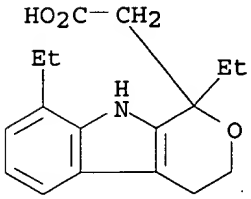
AB As part of our screening program for **cancer** inhibitory agents effective specifically in the promotion stage of **cancer** development, we have evaluated the possible inhibitory effects of 36 non-steroidal anti-inflammatory drugs (NSAIDs) on the Epstein-Barr virus early antigen (EBV-EA) activation which was induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells. All the drugs were obsd. to inhibit the EBV-EA activation at low doses with low toxicity. The two most active anti-tumor promoting agents were the arylacetic acid derivs., etodolac and sulindac. We also report for the first time the activities of 14 new NSAIDs belonging to different classes as potential **cancer** chemopreventive agents. A structure-activity relationship study showed that among the salicylic acid deriv. tested, the oxidn. of the thiol group to dithiol derivs. results in

the redn. of the activity. Introduction of amino group on the salicylic acid mols. also results in the redn. of activity in the EBV-EA assay. The results are of great interest in the development of NSAIDs as **cancer** chemopreventive agents, which halt **cancer** progression in multistage carcinogenesis, where successive activities are required to evolve into fully-fledged and metastatic **cancer**.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAID inhibition of Epstein-Barr virus early antigen activation)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:608551 CAPLUS
DOCUMENT NUMBER: 133:213151
TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050007	A1	20000831	WO 2000-US165	20000105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294192	B1	20010925	US 1999-258654	19990226
NZ 513810	A	20010928	NZ 2000-513810	20000105
EP 1158959	A1	20011205	EP 2000-901394	20000105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537317	T2	20021105	JP 2000-600619	20000105

PRIORITY APPLN. INFO.: US 1999-258654 A 19990226
WO 2000-US165 W 20000105

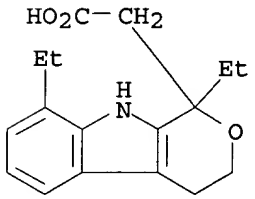
AB The present invention relates to triglyceride-free pharmaceutical compns.

for delivery of hydrophobic therapeutic agents. Compns. of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon diln. with an aq. solvent, the compn. forms a clear, aq. dispersion of the surfactants contg. the therapeutic agent. The invention also provides methods of treatment with hydrophobic therapeutic agents using these compns. A pharmaceutical compn. contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacel186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:351352 CAPLUS
DOCUMENT NUMBER: 132:352823
TITLE: Local delivery of drugs to the colon for local treatment of colonic diseases
INVENTOR(S): Lerner, Itzhak E.; Flashner, Moshe; Penhasi, Adel
PATENT ASSIGNEE(S): Dexxon Ltd., Israel
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000028974	A1	20000525	WO 1999-IL607	19991112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6231888	B1	20010515	US 1998-190127	19981112
EP 1131058	A1	20010912	EP 1999-972097	19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1998-190127	A	19981112
US 1996-588247	A2	19960118
WO 1999-IL607	W	19991112

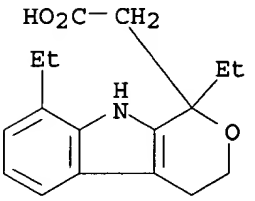
09/ 634,207

AB A compn. and method for the treatment of polyp and colon **cancer** is described, such compn. and method providing for the colonic delivery and/or preferential metab. of a drug or desired agent, esp. an NSAID, in the colon of the patient in need of such treatment. An example is give of a cross-over pilot colonic delivery study including 2 coated sustained-release colonic delivery systems comprising Na diclofenac an Eudragit E and Ca pectinate coatings.

IT **41340-25-4**, Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colon-specific drug delivery systems)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:53386 CAPLUS
DOCUMENT NUMBER: 132:88170
TITLE: Indole or carbazole compounds and their compositions for treatment of chronic lymphocytic **leukemia**
INVENTOR(S): Nardella, Francis A.; Sitzer, Ruth L.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002555	A1	20000120	WO 1999-US15501	19990708
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2336932	AA	20000120	CA 1999-2336932	19990708
AU 9952098	A1	20000201	AU 1999-52098	19990708
EP 1104297	A1	20010606	EP 1999-937222	19990708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002520282	T2	20020709	JP 2000-558815	19990708
NZ 509376	A	20031031	NZ 1999-509376	19990708
US 6573292	B1	20030603	US 2001-720992	20010706
US 2003232874	A1	20031218	US 2003-404943	20030331

PRIORITY APPLN. INFO.: US 1998-92466P P 19980709

US 1998-94878P P 19980729
WO 1999-US15501 W 19990708
US 2001-720992 A1 20010706

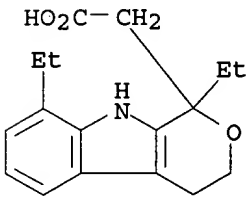
OTHER SOURCE(S): MARPAT 132:88170

AB The level of the leukemic lymphocytes in patients suffering from chronic lymphocytic **leukemia** (CLL) is reduced by the administration of certain indole or carbazole compds., such as the nonsteroidal anti-inflammatory drug etodolac or related indole or carbazole compds. A patient with B-cell CLL was treated with etodolac (300 mg twice daily) for scheduled periods of time, resulting in substantial redns. of the white blood cell count and lymphocyte count, while treatment with other NSAIDs (naproxen, diclofenac, sulindac, nabumetone, oxaprozin, etc.) exhibited relatively little impact on these factors. The platelet count also increased significantly with etodolac.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indole or carbazole compds. and their compns. for treatment of chronic lymphocytic **leukemia**)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:621121 CAPLUS
DOCUMENT NUMBER: 129:239916
TITLE: Therapeutic augmentation of oxyalkylene diesters and butyric acid derivatives with inhibitors of fatty acid .beta.-oxidation
INVENTOR(S): Rephaeli, Ada
PATENT ASSIGNEE(S): Beacon Laboratories, L.L.C., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840078	A1	19980917	WO 1998-US4652	19980311

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

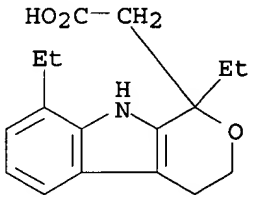
US 5939455	A	19990817	US 1997-814222	19970311
AU 9865478	A1	19980929	AU 1998-65478	19980311
PRIORITY APPLN. INFO.:			US 1997-814222	19970311
			WO 1998-US4652	19980311

AB This invention provides a method of augmenting the therapeutic activity of an oxyalkylene-contg. compd., butyric acid, a butyric acid salt or butyric acid deriv. by administering an inhibitor of .beta.-oxidn. of fatty acids to a patient or to host cells. Pharmaceutical compns. are also included.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxyalkylene diester and butyric acid deriv. therapeutic augmentation with fatty acid .beta.-oxidn. inhibitors)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:621109 CAPLUS
DOCUMENT NUMBER: 129:239915
TITLE: Metabolically stabilized oxyalkylene esters and therapeutic uses thereof
INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada; Neiss, Edward; Loev, Bernard
PATENT ASSIGNEE(S): Beacon Laboratories L.L.C., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840066	A1	19980917	WO 1998-US4753	19980311
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6110955	A	20000829	US 1997-814975	19970311
AU 9864579	A1	19980929	AU 1998-64579	19980311
EP 986380	A1	20000322	EP 1998-910307	19980311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1997-814975 A	19970311

WO 1998-US4753 W 19980311

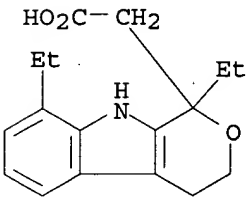
OTHER SOURCE(S): MARPAT 129:239915

AB Compns. for and methods of treating, preventing or ameliorating **cancer** and other proliferative diseases are disclosed, as are methods of inducing wound healing, treating cutaneous ulcers, treating gastrointestinal disorders, treating blood disorders such as anemias, immunomodulation, enhancing recombinant gene expression, treating insulin-dependent patients, treating cystic fibrosis patients, inhibiting telomerase activity, treating virus-assocd. tumors, esp. EBV-assocd. tumors, modulating gene expression and particularly augmenting expression of a tumor suppressor gene, inducing tolerance to an antigen and treating, ameliorating or preventing protozoan infection. The methods of the invention use metabolically stabilized oxyalkylene esters.

IT **41340-25-4D**, Etodolac, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolically stabilized oxyalkylene esters and therapeutic uses thereof)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)

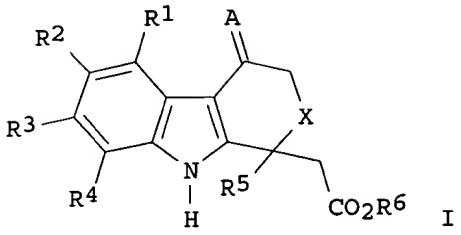


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:457268 CAPLUS
DOCUMENT NUMBER: 129:122569
TITLE: Preparation of pyranoindole inhibitors of COX-2
INVENTOR(S): Kreft, Anthony F.; Caufield, Craig E.; Failli, Amedeo A.; Caggiano, Thomas J.; Greenfield, Alexander A.; Kubrak, Dennis M.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 17 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776967	A	19980707	US 1997-888983	19970707
US 5824699	A	19981020	US 1998-39871	19980316

PRIORITY APPLN. INFO.: US 1997-888983 19970707
OTHER SOURCE(S): MARPAT 129:122569
GI



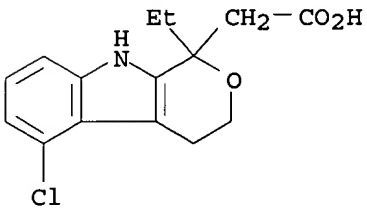
I

AB The title compds. [I; R1-R4 = H, alkyl, alkenyl, etc.; R5 = H, alkyl, alkenyl, alkoxyalkyl, alkylcycloalkyl; R6 = H, alkyl, alkenyl; X = O, C; A = O, NZ; Z = OH, alkoxy, aryloxy, etc.], useful in the treatment of arthritic disorders, colorectal **cancer**, and Alzheimer's disease, were prepd. Thus, treatment of (1-ethyl-1,3,4,9-tetrahydropyrano[3,4-b]indol-1-yl)acetic acid Me ester with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in CH2Cl2/MeOH followed by the hydrolysis of the resulting ester afforded I [R1-R4 = H; R5 = Et; R6 = H; X = O; A = O] which showed IC50 of 2.1 .mu.M against rhCOX-2.

IT **41340-16-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyranoindole inhibitors of COX-2)

RN 41340-16-3 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 5-chloro-1-ethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:341491 CAPLUS
DOCUMENT NUMBER: 129:12742
TITLE: Methods and compositions using thalidomide or other angiogenesis-inhibitory compound and anti-inflammatory agent for inhibition of angiogenesis
INVENTOR(S): D'Amato, Robert J.
PATENT ASSIGNEE(S): Children's Medical Center, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819649	A2	19980514	WO 1997-US20116	19971104
WO 9819649	A3	19980625		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9851973	A1	19980529	AU 1998-51973	19971104
AU 746713	B2	20020502		
EP 963200	A2	19991215	EP 1997-946884	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 336035	A	20020328	NZ 1997-336035	19971104
JP 2002513391	T2	20020508	JP 1998-521728	19971104
US 2003191098	A1	20031009	US 2003-340554	20030110

PRIORITY APPLN. INFO.:
US 1996-28708P P 19961105
US 1997-963058 A 19971103
WO 1997-US20116 W 19971104
US 1999-287377 A1 19990407

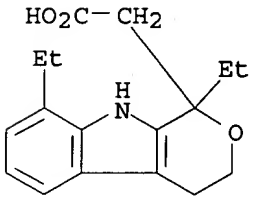
OTHER SOURCE(S): MARPAT 129:12742

AB A group of compds. that effectively inhibit angiogenesis is provided. More specifically, thalidomide and various related compds.,e.g. thalidomide precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit angiogenesis and to treat disease states resulting from angiogenesis. Addnl., antiinflammatory drugs, such as steroids and NSAIDs can inhibit angiogenesis-dependent diseases either alone or in combination with thalidomide and related compds. Importantly, these compds. can be administered orally.

IT **41340-25-4**, Etodolac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thalidomide or other angiogenesis-inhibitory compd. and anti-inflammatory agent for inhibition of angiogenesis)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



L15 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:169432 CAPLUS
DOCUMENT NUMBER: 128:235144
TITLE: Compositions including R-NSAIDS and therapeutic and prophylactic methods employing these compositions
INVENTOR(S): Wechter, William J.; McCracken, John D.
PATENT ASSIGNEE(S): Loma Linda University Medical Center, USA; Wechter, William J.; McCracken, John D.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9809603	A2	19980312	WO 1997-US15940	19970908
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6160018	A	20001212	US 1997-814490	19970310
AU 9744798	A1	19980326	AU 1997-44798	19970908

PRIORITY APPLN. INFO.:
US 1996-706634 A 19960906
US 1997-814490 A 19970310
US 1995-402797 A2 19950313
WO 1997-US15940 W 19970908

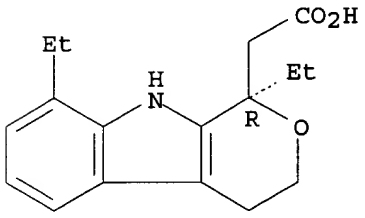
AB A compn. having reduced gastrointestinal toxicity contains an R-NSAID, preferably R-flurbiprofen. The compn. is useful for the treatment of neoplastic diseases such as breast **cancer**, lung **cancer** and **prostate cancer** as well as cystic fibrosis and Alzheimer's disease. R-flurbiprofen was shown to be much less ulcerogenic than its S-enantiomer, yet suppresses cell proliferation in the distal colon.

IT **87226-41-3**, R-Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. R-NSAIDs)

RN 87226-41-3 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro-, (1R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:102847 CAPLUS
DOCUMENT NUMBER: 128:154008
TITLE: Preparation of pyranoindole and carbazole inhibitors of COX-2
INVENTOR(S): Kreft, Anthony Frank, III; Caufield, Craig Eugene; Failli, Amedeo Arturo; Caggiano, Thomas Joseph; Greenfield, Alexander Aleksey; Kubrak, Dennis Michael
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804527	A1	19980205	WO 1997-US12782	19970722
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

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LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,
VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

AU 9740433	A1	19980220	AU 1997-40433	19970722	
EP 923552	A1	19990623	EP 1997-938009	19970722	
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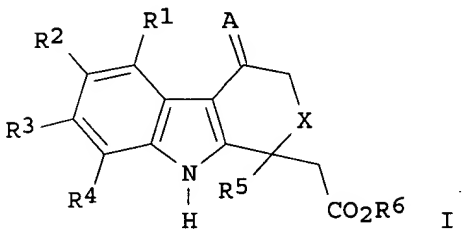
BR 9710597	A	19990817	BR 1997-10597	19970722	
CN 1230948	A	19991006	CN 1997-197994	19970722	
JP 2000515887	T2	20001128	JP 1998-508916	19970722	
ZA 9706611	A	19990125	ZA 1997-6611	19970724	
KR 2000029545	A	20000525	KR 1999-700603	19990125	

PRIORITY APPLN. INFO.: US 1996-687849 A 19960726
WO 1997-US12782 W 19970722

OTHER SOURCE(S): MARPAT 128:154008

GI



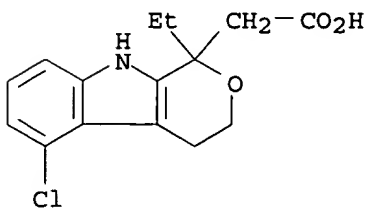
I

AB The title compds. [I; R1-R4 = H, alkyl, alkenyl, etc.; R5 = H, alkyl, alkenyl, alkoxyalkyl, alkylcycloalkyl; R6 = H, alkyl, alkenyl; X = O, C; A = O, NZ; Z = OH, alkoxy, aryloxy, etc.], useful in the treatment of arthritic disorders, colorectal **cancer**, and Alzheimer's disease, were prepd. Thus, reaction of (1-ethyl-1,3,4,9-tetrahydro-pyrano[3,4-b]indol-1-yl)acetic acid Me ester with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in CH2Cl2/MeOH followed by treatment of the intermediate ester with 1N NaOH afforded 95% I [R1-R4 = H; R5 = Et; R6 = H; X = O; A = O] which showed IC50 of 2.1 .mu.M against COX-2.

IT **41340-16-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyranoindole and carbazole inhibitors of COX-2)

RN 41340-16-3 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 5-chloro-1-ethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:681457 CAPLUS
DOCUMENT NUMBER: 125:317341
TITLE: Nonsteroidal anti-inflammatory R-enantiomers for prevention of colorectal **cancer**
INVENTOR(S): Wechter, William J.; Mccracken, John D.
PATENT ASSIGNEE(S): Loma Linda University Medical Center, USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

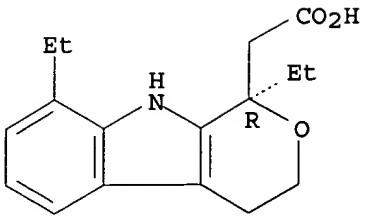
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628148	A2	19960919	WO 1996-US3495	19960313
WO 9628148	A3	19961114		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5955504	A	19990921	US 1995-402797	19950313
CA 2215329	AA	19960919	CA 1996-2215329	19960313
AU 9654227	A1	19961002	AU 1996-54227	19960313
AU 713569	B2	19991202		
EP 814796	A2	19980107	EP 1996-911306	19960313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1183717	A	19980603	CN 1996-192538	19960313
JP 11502199	T2	19990223	JP 1996-527818	19960313
BR 9604881	A	19991130	BR 1996-4881	19960313
BR 9607212	A	19991130	BR 1996-7212	19960313

PRIORITY APPLN. INFO.: US 1995-402797 A 19950313
WO 1996-US3495 W 19960313

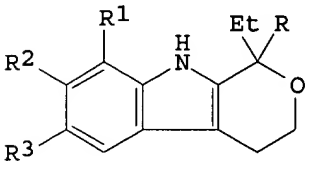
AB A compn. for use in preventing colorectal **cancer** and other neoplastic diseases includes an enantiomerically stable R-NSAID or a pharmaceutically acceptable salt thereof in an amt. effective to elicit a chemoprotective effect. The compn. is substantially free of the S-enantiomer of the R-NSAID. Therapeutic use of the compn. is accompanied by reduced adverse side effects. Guinea pigs were dosed orally with racemic etodolac, S-etodolac, or R-etodolac. Within 24 h after the dose, the animals were euthanized and gross abnormalities were recorded in the GI tract with particular attention to the gastric mucosa of the stomach; based on observations, the R-isomer was seen to cause virtually no gastrointestinal irritation.

IT **87226-41-3**, (-)-Etodolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonsteroidal anti-inflammatory R-enantiomers for prevention of colorectal **cancer**)
RN 87226-41-3 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro-, (1R)-(9CI) (CA INDEX NAME)

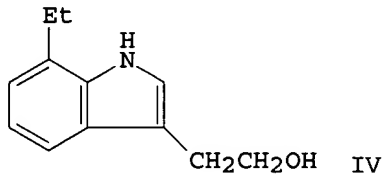
Absolute stereochemistry.



L15 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:178046 CAPLUS
DOCUMENT NUMBER: 114:178046
TITLE: Mutagenicity studies of metabolites, degradation products and impurity of etodolac
AUTHOR(S): Iwakura, Keiko; Tamura, Hironobu; Sumi, Nobuyoshi; Nomura, Akira
CORPORATE SOURCE: Res. Lab., Nippon Shinyaku Co., Ltd., Kyoto, 601, Japan
SOURCE: Oyo Yakuri (1990), 40(6), 747-57
CODEN: OYYAA2; ISSN: 0300-8533
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



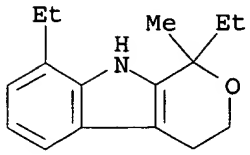
I, R=CH_2CO_2H, R^1=Et, R^2=H, R^3=OH
II, R=CH_2CO_2H, R^1=Et, R^2=OH, R^3=H
III, R=CH_2CO_2H, R^1=CH(OH)Me, R^2=R^3=H
V, R=Me, R^1=Et, R^2=R^3=H
VI, R=CH_2CO_2H, R^1=Me, R^2=R^3=H



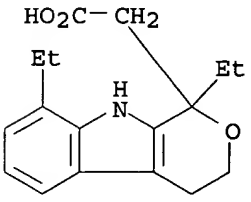
IV

AB RAK-901 (I), RAK-902 (II) and RAK-903 (III) are metabolites of etodolac; RAK-801 (IV) and RAK-802 (V) degrdn. products of etodolac; and the impurity of etodolac RAK-701 (VI) were examd. for mutagenicity in reverse mutation tests on bacteria. In addn., the mutagenicity of II was examd. in a micronucleus test in mice. I, III, IV, V, and VI did not increase revertant colonies in any of the test strains (Salmonella typhimurium TA1535, TA100, TA1537, TA98 and Escherichia coli WP2uvrA) with or without a metabolic activation system (S-9 mix). II, however, increased revertant colonies on S. typhimurium TA1535 in the absence of S-9 mix in the reverse mutation test, but it did not increase micronucleated polychromatic erythrocytes in the bone **marrow** cells of male ddY mice in the micronucleus test.
IT **115066-03-0**, RAK 802
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mutagenicity of, as etodolac degrdn. product)
RN 115066-03-0 CAPLUS
CN Pyrano[3,4-b]indole, 1,8-diethyl-1,3,4,9-tetrahydro-1-methyl- (9CI) (CA

INDEX NAME)



L15 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:156810 CAPLUS
DOCUMENT NUMBER: 114:156810
TITLE: Mutagenicity studies of etodolac. (3). Micronucleus test on mice
AUTHOR(S): Iwakura, Keiko; Tamura, Hironobu; Sumi, Nobuyoshi; Nomura, Akira
CORPORATE SOURCE: Res. Lab., Nippon Shinyaku Co., Ltd., Kyoto, 601, Japan
SOURCE: Oyo Yakuri (1990), 40(6), 733-6
CODEN: OYYAA2; ISSN: 0300-8533
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Etodolac, a new nonsteroidal anti-inflammatory drug, was examd. for mutagenicity in the micronucleus test on mice. When administered orally to Slc:ddY male mice at doses of 60, 120, 240 and 840 mg/kg, the drug did not increase micronucleated polychromatic erythrocytes in the bone **marrow**.
IT **41340-25-4**, (.+-.)-Etodolac
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (mutagenicity of)
RN 41340-25-4 CAPLUS
CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



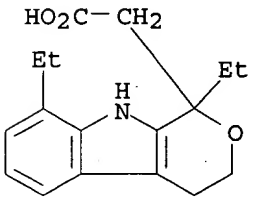
L15 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:171201 CAPLUS
DOCUMENT NUMBER: 110:171201
TITLE: Prostaglandins in inflammatory bone pathology: mechanism and therapeutic benefit of etodolac
AUTHOR(S): Hayward, M. A.; Howard, G. A.; Neuman, R. G.; Wood, D. D.; Weichman, B. M.; Van Sickle, D. C.
CORPORATE SOURCE: Wyeth-Ayerst Res., Princeton, NJ, 08543, USA
SOURCE: Agents and Actions (1989), 26(3-4), 310-18
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To investigated the role of PGE2 in the development of bone and joint pathol. in rat adjuvant arthritis, hindlimb paws were evaluated by calcified tissue histol. techniques focusing on histochem. visualization

of cartilage and bone lesions. Case studies of hindlimbs from normal, adjuvant arthritic, and etodolac-treated arthritic rats demonstrated the assocn. of disease severity with inflammation, chondromalacia, replacement of adipose bone **marrow** with a fibroid **marrow**, osteoclastic bone resorption, synovial cysts, and pannus formation within the joints. Extensive periosteal intramembranous bone formation was temporally assocd. with joint destruction and medullary tissue pathol. In vivo data were correlated with in vitro effects of inflammatory mediators (IL-1, PGE2) on bone resorption. Etodolac blocked bone explant PGE2 accumulation at concns. of 10-7M and higher, and inhibited bone resorption at concns. of 10-5M and higher. The data indicate that in vitro and in vivo models of bone metab. are well correlated regarding prostaglandin synthesis; that the inflammatory mediator PGE2 is largely responsible for the involvement of skeletal tissue in the adjuvant arthritis model; and that the effects of etodolac are specifically mediated by its ability to inhibit PGE2 accumulation in vivo.

IT **41340-25-4**
RL: BIOL (Biological study)
(adjuvant arthritis response to, prostaglandin in)

RN 41340-25-4 CAPLUS

CN Pyrano[3,4-b]indole-1-acetic acid, 1,8-diethyl-1,3,4,9-tetrahydro- (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 13:20:13 ON 06 JAN 2004)

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L1		STRUCTURE UPLOADED
L2	1256	S L1 FUL
L3	6	S MITOXANTRONE
L4	40	S PREDNISONE
L5	13	S ESTRAMUSTINE
L6	17	S MELPHALAN
L7	155	S VINBLASTINE
L8	0	S BICAFUTAMIDE
L9	0	S BICAFLUTAMIDE
L10	1	S NILUTAMIDE
L11	5	S FLUTAMIDE

FILE 'CAPLUS' ENTERED AT 13:26:29 ON 06 JAN 2004

L12	700	S L2
L13	4	S L12 AND (CARBONYL OR CARBOXYL OR SULFONYL OR SULPHONYL)
L14	696	S L12 NOT L13
L15	41	S L14 AND (CANCER? OR LEUKEMIA OR MYELOMA OR PROSTATE OR HEMATO

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	[redacted]	[redacted]